Maximum or Mean: That Is the Question

Kei Asayama, Takayoshi Ohkubo, Lutgarde Thijs, Masahiro Kikuya, Jan A. Staessen and Yutaka Imai

Hypertension published online August 1, 2011
Hypertension is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0194-911X. Online ISSN: 1524-4563

Letter to the Editor

Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1000 words (typed double-spaced) in length and may be subject to editing or abridgment.

Maximum or Mean: That Is the Question

To the Editor:

Recently, Matsui et al[1] suggested that maximum home systolic blood pressure (SBP) might enhance the predictive value of mean SBP in relation to hypertensive target organ damage in the heart and arteries. However, the data presented do not wholly substantiate the conclusions of Matsui et al.[1] First, because of the collinearity problem between maximum and mean SBP, the results for the total population in Table 3 of their study[1] should have been omitted. Second, the reader is also left without any information on the contribution of maximum SBP in explaining the variance in left ventricular mass index and carotid intima-media thickness, because in their Table 3[1] only the whole-model R^2 was given. Third, because of the cross-sectional design and the use of intermediate signs of target organ damage, we suggest that the term "prediction," as used, for instance, in the conclusion of their Abstract,[1] is inappropriate. Finally, the maximum morning SBP was recorded during the first 3 days in more than one third of the patients studied by Matsui et al.[1] We find it counterintuitive that a measurement obtained within 3 days of self-measurement at home would be more closely associated with target organ damage than the mean level of blood pressure recorded over 14 days.

In trying to replicate the observations of Matsui et al,[1] we evaluated whether, in 2354 Ohasama participants[2] followed up for 12.1 years (median), maximum home SBP (single measurements in the morning for ≤28 days) predicted cardiovascular mortality (144 deaths). In multivariable-adjusted Cox regression, the standardized hazard ratios associated with the maximum and mean home SBP at home were 1.30 (95% CI: 1.08 to 1.57; $P=0.006$) and 1.28 (95% CI: 1.08 to 1.53; $P=0.006$), respectively. The correlation coefficient between maximum and mean SBP was 0.91 ($P<0.001$). Adding maximum home SBP, therefore, did not improve a Cox model that included mean SBP, as indicated by the likelihood ratio test (likelihood ratio: 0.49; $P=0.48$) and vice versa (likelihood ratio: 0.46; $P=0.50$). In conclusion, we do not believe that the results from Matsui et al[1] overrule the current recommendations to measure the home blood pressure over ≥7[3] days and to use the mean level for risk stratification.

Sources of Funding

This study was supported in part by Grants for Scientific Research (18390192, 18590587, 19590929, 19790423, 20590629, 21390201, 21591016, 22590767, 22790556, 22890017, 23249036 and 23790242) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan; Grant-in-Aid (H18-Junkankitou[Seishuu]-Ippan-012, H20-Junkankitou[Seishuu]-Ippan-009, 013 and H23-Junkankitou[Senshuu]-Ippan-005) from the Ministry of Health, Labor and Welfare, Health and Labor Sciences Research Grants, Japan; Grant-in-Aid for Japan Society for the Promotion of Science (JSPS) fellows (18.54042, 19.7152, 20.7198, 20.7477 and 20.54043); Health Science Research Grants and Medical Technology Evaluation Research Grants from the Ministry of Health, Labor and Welfare, Japan; Japan Arteriosclerosis Prevention Fund; Biomedical Innovation Grants; a Grant from the Miso Central Institute, Tokyo, Japan; and a Grant from the Sendai Knowledge Cluster Initiative, Sendai, Japan.

Disclosures

None.

Kei Asayama
Studies Coordinating Centre
Division of Hypertension and Cardiovascular Rehabilitation
Department of Cardiovascular Diseases
University of Leuven
Leuven, Belgium
Department of Planning for Drug Development and Clinical Evaluation
Tohoku University Graduate School of Pharmaceutical Sciences
Sendai, Japan

Takayoshi Ohkubo
Department of Planning for Drug Development and Clinical Evaluation
Tohoku University Graduate School of Pharmaceutical Sciences
Sendai, Japan
Department of Health Science
Shiga University of Medical Science
Otsu, Japan

Lutgarde Thijs
Studies Coordinating Centre
Division of Hypertension and Cardiovascular Rehabilitation
Department of Cardiovascular Diseases
University of Leuven
Leuven, Belgium

Masahiro Kikuya
Department of Planning for Drug Development and Clinical Evaluation
Tohoku University Graduate School of Pharmaceutical Sciences
Sendai, Japan

Jan A. Staessen
Studies Coordinating Centre
Division of Hypertension and Cardiovascular Rehabilitation
Department of Cardiovascular Diseases
University of Leuven
Leuven, Belgium
Department of Epidemiology
Maastricht University
Maastricht, the Netherlands

This paper was sent to John E. Hall, associate editor, for review by expert referees, editorial decision, and final disposition.
(*Hypertension*. 2011;58:e13-e14.)

Yutaka Imai
Department of Planning for Drug Development and Clinical Evaluation
Tohoku University Graduate School of Pharmaceutical Sciences
Sendai, Japan

1. Matsui Y, Ishikawa J, Eguchi K, Shibasaki S, Shimada K, Kario K. Maximum value of home blood pressure: a novel indicator of target organ damage in hypertension. *Hypertension*. 2011;57:1087–1093.
2. Kikuya M, Ohkubo T, Metoki H, Asayama K, Hara A, Obara T, Inoue R, Hoshi H, Hashimoto J, Totsune K, Satoh H, Imai Y. Day-by-day variability of blood pressure and heart rate at home as a novel predictor of prognosis: the Ohasama Study. *Hypertension*. 2008;52:1045–1050.
3. Parati G, Stergiou GS, Asmar R, Bilo G, de Leeuw P, Imai Y, Kario K, Lurbe E, Manolis A, Mengden T, O'Brien E, Ohkubo T, Padfield P, Palatini P, Pickering T, Redon J, Revera M, Ruilope LM, Shennan A, Staessen JA, Tisler A, Waeber B, Zanchetti A, Mancia G. European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home Blood Pressure Monitoring. *J Hypertens*. 2008;26:1505–1526.

Response to Maximum or Mean: That Is the Question

Yoshio Matsui, Joji Ishikawa and Kazuomi Kario

Hypertension published online August 1, 2011
Hypertension is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514
 Print ISSN: 0194-911X. Online ISSN: 1524-4563

Letter to the Editor

Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1000 words (typed double-spaced) in length and may be subject to editing or abridgment.

Response to Maximum or Mean: That Is the Question

We thank Asayama et al[1] for their remarks about our recent article[2] and for showing their valuable data. We could not perform a simple comparison of our results with those of the Ohasama Study[3] because there are several differences in the subjects' characteristics and study design between our study and the Ohasama Study,[2,3] as follows: (1) elderly untreated hypertensives versus general population including treated hypertensives; (2) the average age of the subjects (67 years versus 59 years); (3) the primary end point (target organ damage versus cardiovascular mortality); and (4) the blood pressure (BP) measurement schedule at home (3 times each in the morning and evening for 2 weeks versus once in the morning over a period of 4 weeks). Here, we will try to answer the 4 main points raised in their letter.

First, we think that Asayama et al[1] misunderstood the analysis of our article. As described in our Methods section, we did not include the maximum home systolic BP (SBP) and mean home SBP together in the same multivariable model because of multicollinearity. Therefore, we think that the results for the total population should not be omitted.

Second, the square of partial correlation coefficient of left ventricular mass index was 0.104 ($P<0.001$) in the total population, 0.055 ($P=0.007$) in the lower home BP group, and 0.086 ($P<0.001$) in the higher home BP group; that of carotid intima-media thickness was 0.084 ($P<0.001$), 0.059 ($P=0.006$), and 0.083 ($P<0.001$), respectively.

Third, we agree that the term "prediction" might have been inappropriate in a cross-sectional study. In our article, we meant to speculate on the presence of target organ damage from maximum home SBP in hypertensive patients.

Fourth, although 39% of all subjects had their maximum home SBP on the first 3 days, our results did not necessarily indicate that home BPs during the first 3 days are sufficient for assessment of the association between home BP and target organ damage.

In addition, in this article, we did not deny the recommendation of the current home BP guideline[4] to measure the home BP over ≥7 days and to use the mean home BP level for risk stratification. What we would like to emphasize here was that the maximum value of home SBP could add further information about the potential severity of target organ damages to the mean level of home SBP. We are now prospectively studying the predictive value of the maximum and mean home SBP for cardiovascular mortality in our hypertensive cohort in an attempt to clarify whether the significance of the maximum home SBP may differ depending on the characteristics of the study subjects.

Sources of Funding

This study was supported in part by a research grant by Omron Healthcare, Co, Ltd (Kyoto, Japan).

Disclosures

None.

Yoshio Matsui
Joji Ishikawa
Kazuomi Kario
Division of Cardiovascular Medicine
Department of Medicine
Jichi Medical University School of Medicine
Tochigi, Japan

1. Asayama K, Ohkubo T, Thijs L, Kikuya M, Staessen JA, Imai Y. Maximum or mean: that is the question. *Hypertension.* 2011;58:e13–e14.
2. Matsui Y, Ishikawa J, Eguchi K, Shibasaki S, Shimada K, Kario K. Maximum value of home blood pressure: a novel indicator of target organ damage in hypertension. *Hypertension*. 2011;57:1087–1093.
3. Kikuya M, Ohkubo T, Metoki H, Asayama K, Hara A, Obara T, Inoue R, Hoshi H, Hashimoto J, Totsune K, Satoh H, Imai Y. Day-by-day variability of blood pressure and heart rate at home as a novel predictor of prognosis: the Ohasama Study. *Hypertension*. 2008;52:1045–1050.
4. Parati G, Stergiou GS, Asmar R, Bilo G, de Leeuw P, Imai Y, Kario K, Lurbe E, Manolis A, Mengden T, O'Brien E, Ohkubo T, Padfield P, Palatini P, Pickering T, Redon J, Revera M, Ruilope LM, Shennan A, Staessen JA, Tisler A, Waeber B, Zanchetti A, Mancia G, for the ESH Working Group on Blood Pressure Monitoring. European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home Blood Pressure Monitoring. *J Hypertens.* 2008;26:1505–1526.

(*Hypertension*. 2011;58:e15.)

Hypertension is available at http://hyper.ahajournals.org DOI: 10.1161/HYPERTENSIONAHA.111.178566